

(19) World Intellectual Property
Organization
International Bureau



20 JUN 2005

(43) International Publication Date
15 July 2004 (15.07.2004)

PCT

(10) International Publication Number
WO 2004/058050 A3

- (51) International Patent Classification⁷: **C12Q 1/68**,
G01N 33/53, 33/566, A01N 61/00, A61K 39/395
- (21) International Application Number:
PCT/US2003/040701
- (22) International Filing Date:
19 December 2003 (19.12.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/434,918 20 December 2002 (20.12.2002) US
60/463,577 17 April 2003 (17.04.2003) US
- (71) Applicant (for all designated States except US): **AVALON PHARMACEUTICALS** [US/US]; 20358 Seneca Meadows Parkway, Germantown, MD 20876 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **AUGUSTUS, Meena** [IN/IN]; 3215 Hollyhock Drive, Burtonsville, MD 20866 (US). **HORRIGAN, Stephen** [US/US]; 1895 Milboro Drive, Potomac, MD 20854 (US). **CAIN, Colyn** [US/US]; 4309 Kentbury Drive, Bethesda, MD 20814 (US). **STROVEL, Jeffrey, W.** [US/US]; 14622 Keeneland Circle, North Potomac, MD 20878 (US).
- (74) Agents: **GRANT, Alan, J.** et al.; Carella, Byrne, Bain, Gilfillan, Cecchi, Stewart &, Olstein, 5 Becker Farm Road, Roseland, NJ 07068 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (88) Date of publication of the international search report:
10 February 2005
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **AMPLIFIED CANCER TARGET GENES USEFUL IN DIAGNOSIS AND THERAPEUTIC SCREENING**

(57) Abstract: A gene useful as a prognostic indicator of survival of patients afflicted with cancers such as breast cancer is described. Also disclosed are methods for screening potential therapeutic agents, such as antitumor agents, based on their modulation of the expression of a TRIP13 gene, or splice variants thereof, along with methods for diagnosing cancerous, or potentially cancerous, conditions as a result of the expression, or patterns of expression, of such genes, including changes in copy number. Also disclosed are methods for detecting or determining functionally related genes, where disruption of TRIP13 may affect such related-gene expression, as well as methods for treating cancer based on targeting expression products of such genes and determining genes involved in the cancerous process. Methods for identifying, detecting and following patients and others having high levels of amplification/expression of the gene before treatment where differences after treatment serve as markers for indication of success of treatment or for identifying individuals who would benefit from such treatment using this gene marker as a diagnostic and/or prognostic and/or pharmacodynamic or surrogate marker are described.

WO 2004/058050 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/40701

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; G01N 33/53, 33/566; A01N 61/00; A61K 39/395
US CL : 435/6, 7.1; 436/501; 514/1; 424/138.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6, 7.1; 436/501; 514/1; 424/138.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LEE et al. Two clases of proteins dependent on either the presence or absence of thyroid hormone for interaction with the thyroid hormone receptor. Molecular Endocrinology. 1995, Vol. 9, No. 2, pages 243-254, see table 2, trip 13.	1-59
Y	WO 02/061134 A2 (BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS) 08 August 2002 (08.08.2002), see pages 7 and 8.	1, 21, 46
Y	CHANG et al. Molecular determinants of terminal growth arrest induced in tumor cells by a chemotherapeutic agent. Proc. Natl. Acad. Sci. 08 January 2002, Vol. 99, No. 1, pages 389-394, see figure 2, last gene.	1-59
Y	US 6346,605 B1 (LEE et al) 12 February 2002 (12.02.2002), see column 6, lines 30-45, lines 52-67, column 12, lines 24-43.	1-59
Y	US 6,271,349 B1 (DOUGALL et al) 07 August 2001 (07.08.2001), see column 2.	1-59
Y	WO 00/18959 A1 (THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK) 06 April 2000 (06.04.2000), see entire document.	1-59

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents:	
A document defining the general state of the art which is not considered to be of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
E earlier application or patent published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
O document referring to an oral disclosure, use, exhibition or other means	*Z* document member of the same patent family
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

28 October 2004 (28.10.2004)

Date of mailing of the international search report

22 NOV 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Jeffrey Fredman

Telephone No. (571) 272-1600

INTERNATIONAL SEARCH REPORT

PCT/US03/40701

Continuation of B. FIELDS SEARCHED Item 3:

EAST, MEDLINE, CAPLUS, BIOSIS

search terms: TRAF, TRIP, cancer, carcinogen, tumor, neoplastic, malignant, drug, compound, screen, identify